

REMARKS

Favorable reconsideration of this application in light of the preceding amendments and the following discussion is respectfully requested.

No claims having been cancelled or added, the Applicants respectfully submit that claims 15-20 and 52-65 remain properly under consideration in this application. The above Amendment shows the amended claims in marked-up form in accordance with 37 C.F.R. § 1.121.

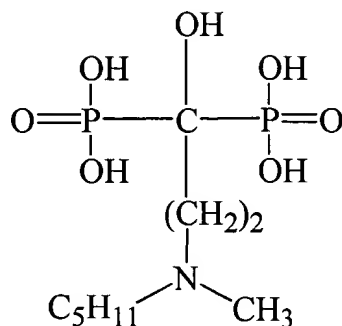
The Applicant notes with appreciation the Examiner's acknowledgement that all certified copies of the documents from which priority is claimed under 35 U.S.C. § 119 have been received.

The Applicant further notes with appreciation the Examiner's return of an initialed copy of the information disclosure materials received October 28, 2002, and January 31, 2003, as papers 19 and 22 respectively.

Rejections Under 35 U.S.C. § 103(a)

Claims 15-20 and 52-65 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Lyons et al.'s British Patent No. 2312165 ("Lyons") in view of Michael et al.'s U.S. Patent No. 6,174,520 ("Michael"). The Applicant respectfully traverses this rejection and requests that it be withdrawn.

The Applicant respectfully maintains that Lyons is directed to the use of a specific bisphosphonate, ibandronate,



IBANDRONATE

for the suppression of inflammatory reactions such as chronic immune system activation and as an alternative to the use of systemic corticosteroids, cyclophosphamide and cyclosporin. Lyons at 2. The Applicant respectfully contends, therefore, that one of ordinary skill would understand that Lyons is directed to the treatment of a particular symptom of diseases by inhibiting interleukin-8 (IL-8) secretions. Indeed, Lyons suggests that ibandronate specifically targets the tumor necrosis factor (TNF) and IL-8 pathway to inhibit the production of these pro-inflammatory cytokines. Lyons at 4-5. The Applicant respectfully maintains, however, that Lyons does not teach or suggest that the combination of ibandronate with any allergen or antigen would provide any benefit in the treatment of allergies or autoimmune disorders.

The Applicant respectfully contends that Michael is directed to a means for the oral administration of therapeutic proteins utilizing an acid-stable coating to protect the proteins during their passage through the stomach and provide for their release in the small intestine. The Applicant respectfully maintains, however, that Michael does not teach or suggest that the combination of the therapeutic proteins with ibandronate,

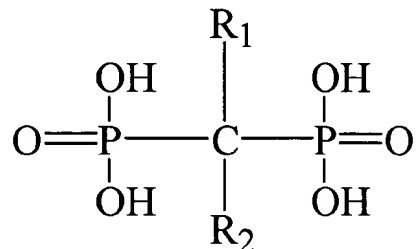
bisphosphonates in general or any other compound would suppress the body's reaction to the therapeutic protein.

Indeed, the Applicant respectfully contends that Michael's use of the therapeutic proteins is intended to "activate the immune system," col. 1, line 60 to col. 2, line 12, rather than suppress the immune response. With respect to Michael's suggestion that certain autoimmune disorders, particularly multiple sclerosis (MS) through the administration of myelin basic protein (MBP), the Applicant respectfully contends that subsequent work in the field, particularly the Brod and Wiendl references provided with the Applicant's 2003 IDS, indicate that such therapies are not effective. The Applicant respectfully contends that one of ordinary skill in the art, having knowledge of Brod and Wiendl, would not be led to utilize the teachings of Michael in the manner suggested and would not, therefore, have been motivated to produce the present invention.

The Applicant respectfully contends, therefore, that Lyons addresses the treatment of a particular symptom, inflammation, that may result from an autoimmune disorder, but does not teach or suggest that such a compound may be used to treat the underlying disease. Conversely, Michael addresses the intestinal delivery of therapeutic proteins designed to activate the immune system and does not, therefore, teach or suggest the corresponding administration of a compound for suppressing the immune system response. The Applicant further respectfully maintains that neither of the applied references teach or suggest that a combination of such materials would have a synergistic, rather than additive, effect in the treatment of autoimmune disorders.

The Applicant also respectfully contends that the claimed compounds, particularly those recited in claims 58-65, are materially different from the ibandronate taught by

Lyons. The Applicant further contends that those of ordinary skill in the art appreciate that each bisphosphonic acid (and related bisphosphonate)



BISPHOSPHONIC ACID

has a generally unique activity profile determined by the structure of the side chains R_1 and R_2 , and that the teachings of Lyons would not be understood to extend to the range of bisphosphonates recited in the present claims.

For the reasons detailed above, the Applicant respectfully maintains that, when the applied references are considered as a whole, their teachings are insufficient to support the proposed combination. The Applicant, therefore, requests that this rejection be withdrawn.

CONCLUSION


In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections have been addressed and overcome, leaving the present application in condition for allowance. A notice to that effect is respectfully requested.

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge any underpayment or non-payment of any fees required under 37 C.F.R. §§ 1.16 or 1.17, or credit any overpayment of such fees, to Deposit Account No. 08-0750, including, in particular, extension of time fees.

Very truly yours,

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